



Patent
45198.00027.RCE2(CON1)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Erion *et al.*

Serial No.: 09/978,454

Filed: October 15, 2001

Title: **NOVEL PRODRUGS FOR
PHOSPHORUS-CONTAINING
COMPOUNDS**

Group Art Unit: 1616

Examiner: Dameron Jones

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR § 1.97(b)(3)

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Sir:

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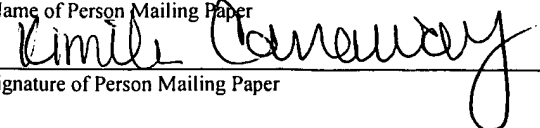
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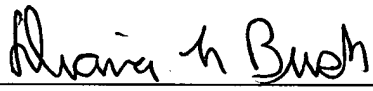
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Respectfully submitted,

Dated: 1/30/04

By: 
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 3

Complete if Known

Application Number 09/978,454
Filing Date October 15, 2001
First Named Inventor Erion et al.
Group Art Unit 1616
Examiner Name Dameron Jones
Attorney Docket Number 032465.00027.RCE2(CON1)

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
	AA	6,054,587	1	Reddy et al.	04/25/00	
	AB	6,110,903	1	Kasibhatla et al.	08/29/00	
	AC	6,284,748	1	Dang et al.	09/04/01	
	AD	6,294,672	1	Reddy et al.	09/25/01	
	AF	6,399,782	1	Kasibhatla et al.	06/04/02	
	AE	6,489,476	1	Dang et al.	12/03/02	

FOREIGN PATENT DOCUMENTS

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		Beaucage and Iyer, "The Synthesis of Modified Oligonucleotides by the Phosphoramidite Approach and Their Applications," <u>Tetrahedron</u> , 49(28):6123-6194 (1993).	
		Borch and Millard, "The Mechanism of Activation of 4-Hydroxycyclophosphamide," <u>J. Med. Chem.</u> , 30:427-431 (1987).	
		Cooper et al., "Use of Carbohydrate Derivatives for Studies of Phosphorus Stereo-chemistry. Part II. Synthesis and Configurational Assignments of 1,3,2-Oxathiaphosphorinan-2-ones and 1,3,2-Dioxaphosphorinan-2-thiones," <u>J.C.S. Perkin I</u> , 3/2422:1049-1052 (1973).	
		Clercq et al., "A Novel Selective Broad-spectrum Anti-DNA Virus Agent," <u>Nature</u> , 323:464-467 (1986).	

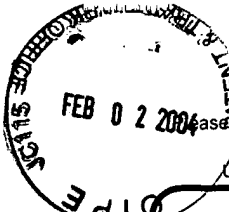
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		Application Number	09/978,454		
		Filing Date	October 15, 2001		
		First Named Inventor	Erion et al.		
		Group Art Unit	1616		
		Examiner Name	Dameron Jones		
Sheet	2	of	3	Attorney Docket Number	032465.00027.RCE2(CON1)

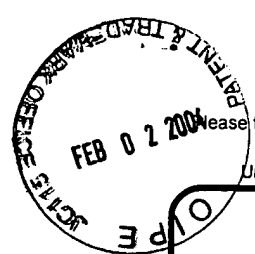
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		Farquhar et al., "Synthesis and Antitumor Evaluation of Bis[(pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <u>J. Med. Chem.</u> , 37:3902-3909 (1994).	
		Friis and Bundgaard, "Prodrugs of Phosphates and Phosphonates: Novel Lipophilic α -acyloxyalkyl Ester Derivatives of Phosphate- or Phosphonate Containing Drugs Masking the Negative Charges of these Groups," <u>Euro. J. Pharm. Sci.</u> , 4:49-59 (1996).	
		Harada et al., "Resolution of 1,3-alkanediols Via Chiral Spiroketal Derived from ι -Menthone," <u>Tetrahedron</u> , 28(41):4843-4846 (1987).	
		Khorana et al., "Cyclic Phosphates. III. Some General Observations on the Formation and Properties of Five-, Six- and Seven-membered Cyclic Phosphate Esters," <u>Brit. Col. Res. Couns.</u> , 79:430-436 (1957).	
		Korba et al., "Liver-targeted Antiviral Nucleosides: Enhanced Antiviral Activity of Phosphatidyl-dideoxyguanosine Versus Dideoxyguanosine in Woodchuck Hepatitis Virus Infection <i>In Vivo</i> ," <u>Hepatology</u> , 23(5):958-963 (1996).	
		Lefebvre et al., "Mononucleoside Phosphotriester Derivatives with <i>S</i> -acyl-2-thioethyl Bioreversible Phosphate-protecting Groups: Intracellular Delivery of 3'-azido-2',3'-dideoxythymidine 5'-monophosphate," <u>J. Med. Chem.</u> , 38:3941-3950 (1995).	
		Ludeman et al., "Synthesis and Antitumor Activity of Cyclophosphamide Analogues. 4. Preparation, Kinetic Studies, and Anticancer Screening of "Phenylketophosphamide" and Similar Compounds Related to the Cyclophosphamide Metabolite Aldophosphamide," <u>J. Med. Chem.</u> , 29:716-727 (1986).	
		McGuigan et al., "Intracellular Delivery of Bioactive AZT Nucleotides by Aryl Phosphate Derivatives of AZT," <u>J. Med. Chem.</u> , 36:1048-1052 (1993).	
		Mosbo and Verkade, "Dipole Moment, Nuclear Magnetic Resonance, and Infrared Studies of Phosphorus Configurations and Equilibria in 2-R-2-Oxo-1,3,2-dioxaphosphorinanes," <u>J. Org. Chem.</u> , 42(9):1549-1555 (1977).	
		Nakayama and Thompson, "A Highly Enantioselective Synthesis of Phosphate Triesters," <u>J. Am. Chem. Soc.</u> , 112:6936-3942 (1990).	

Examiner Signature	Date Considered
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		First Named Inventor	Erion et al.
		Group Art Unit	1616
		Examiner Name	Dameron Jones
		Attorney Docket Number	032465.00027.RCE2(CON1)
Sheet	3	of	3

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		Ramachandran et al., "Efficient General Synthesis of 1,2- and 1,3-diols in High Enantiomeric Excess via the Intramolecular Asymmetric Reduction of the Corresponding Ketoalkyl Diisopinocampheylborinate Intermediates," <u>Tetrahedron</u> , 38(5):761-764 (1997).	
		Starrett, Jr. et al., "Synthesis, Oral Bioavailability Determination, and <i>in Vitro</i> Evaluation of Prodrugs of the Antiviral Agent 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA)," <u>J. Med. Chem.</u> , 37:1857-1864 (1994).	
		Thompson et al., "Synthesis, Bioactivation and Anti-HIV Activity of the Bis(4-acyloxybenzyl) and Mono(4-acyloxybenzyl) Esters of the 5'-monophosphate of AZT," <u>J. Chem. Soc.</u> , 2/06723D:1239-1245 (1993).	
		Weber and Waxman, "Activation of the Anti-cancer Drug Ifosfamide by Rat Liver Microsomal P450 Enzymes," <u>Biochem. Pharm.</u> , 45(8):1685-1694 (1993).	
		Zon et al., "NMR Spectroscopic Studies of Intermediary Metabolites of Cyclophosphamide. A Comprehensive Kinetic Analysis of the Interconversion of <i>cis</i> - and <i>trans</i> -4-Hydroxycyclophosphamide with Aldophosphamide and Concomitant Partitioning of Aldophosphamide Between Irreversible Fragmentation and Reversible Conjugation Pathways," <u>J. Med. Chem.</u> 27:466-485 (1984).	

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